


Titre	Étude ouverte multicentrique portant sur l'augmentation et l'expansion de la dose visant à évaluer l'innocuité, la tolérabilité, la dosimétrie et l'efficacité préliminaire du radioligand CAM-H2 dirigé contre le gène HER2 chez les patients atteints d'un cancer du sein, de l'estomac ou de la jonction gastro-œsophagienne HER2 positif avancé ou métastatique
Protocole ID	CAMH2-1001
ClinicalTrials.gov ID	NCT04467515
Type(s) de cancer	Estomac Sein
Phase	Phase I-II
Type étude	Clinique
Médicament	CAM-H2 Radioligand
Institution	CENTRE UNIVERSITAIRE DE SANTE MCGILL  SITE GLEN 1001 boul. Décarie , Montréal, QC, H4A 3J1
Ville	
Investigateur principal	Dr Catalin Mihalciou
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Statut	Actif en recrutement
But étude	This is a Phase 1/2 multi-center, open label, dose escalation and dose expansion study to evaluate safety, tolerability, dosimetry, pharmacodynamics (PD), and efficacy of the targeted radionuclide therapeutic CAM-H2 in patients with progressive, advanced/metastatic HER2-positive breast, gastric, and GEJ cancer with disease progression following anti-HER2 standard of care treatment. The study duration for each phase will be up to 18 months. The study is comprised of a Treatment Period, consisting of a maximum of 2 cycles (12 weeks per cycle) of study drug, and a 12-month Long-Term Follow-Up Period.
Critères d'éligibilité	<ul style="list-style-type: none">• Informed consent form signed voluntarily before any study-related procedure is performed, indicating that the patient understands the purpose of, and procedures required for, the study and is willing to participate in the study.• Males and females \geq 18 years of age.• Eastern Cooperative Oncology Group performance status of 0 to 1.• HER2-positive locally advanced or metastatic breast cancer refractory to standard cancer treatment or HER2-positive locally advanced or metastatic gastric or GEJ cancer, refractory to standard cancer treatment.• Patients should have a minimum of 1 measurable lesion on computed tomography (CT) or magnetic resonance imaging (MRI) as defined by RECIST version 1.1 within 4 weeks of the first dose of the study drug (Day 1). The lesion has to be a new lesion or progression of an existing lesion under the current therapy.• Patients with brain metastases should have a minimum of 1 measurable lesion on MRI as defined by RANO-BM within 4 weeks of the first dose of the study drug (Day 1). The lesion has to be a new lesion or progression of an existing lesion under the current therapy.• Any previous anti-HER2 treatment for advanced or metastatic disease is allowed. Patients with breast cancer should have had at least 2 previous systemic anticancer treatments for recurrent, locally advanced or metastatic cancer. Patients with gastric cancer or GEJ cancer should have had at least 1 previous anti-HER2 treatment.• Life expectancy $>$ 6 months.• Adequate organ function, determined by the following laboratory tests performed within 21 days

before screening:

- Adequate kidney function with an estimated creatinine clearance of > 60 mL/min (Chronic Kidney Disease Epidemiology Collaboration formula).
- Adequate hepatic function defined as an alanine aminotransferase (ALT) and aspartate aminotransferase (AST) < 2.5 the upper limit of normal (ULN), or < 5 ULN in patients with liver metastases, and total bilirubin $< 2 \times$ ULN.
- Baseline left ventricular ejection fraction $\geq 50\%$ as measured by echocardiography or multigated acquisition scan.
- Absence of any psychological, family, sociological, or geographical circumstance that could potentially represent an obstacle to compliance with the study protocol and the follow-up schedule, as determined by the Investigator. These circumstances will be discussed with the patient before enrollment in the study.
- Female patients of childbearing potential (ie, ovulating, premenopausal, and not surgically sterile) must have a negative serum pregnancy test within 7 days prior to administration of study drug. Patients and their partners of childbearing potential must be willing to use 2 methods of contraception, 1 of which must be a barrier method, for the duration of the study and should be maintained until 6 months after study drug administration. Medically acceptable barrier methods include condom with spermicide or diaphragm with spermicide. Medically acceptable non-barrier contraceptive methods include intrauterine devices or hormonal contraceptives (oral, implant, injection, ring, or patch).

Critères d'exclusion

- Presence of frank leptomeningeal disease as a unique central nervous system feature or in association with brain parenchymal measurable lesion(s).
- Symptomatic brain metastases. Note: Patients with asymptomatic treated and untreated brain metastases are eligible.
- Previous local therapy for brain metastases, such as neurosurgery, stereotactic radiotherapy, or whole brain radiotherapy, administered within 6 weeks prior to administration of CAM-H2. Note: Previous therapy for brain metastases administered at least 6 weeks prior to CAM-H2 administration will be permitted.
- For patients with brain metastases, any increase in corticosteroid dose during the week prior to enrollment. Note: Corticosteroid treatment in a stable dose or decreasing dose for at least 4 weeks prior to enrollment is allowed.
- Uncontrolled intercurrent illness including, but not limited to, ongoing or active infection requiring parenteral antibiotics or psychiatric illness/social situations that would limit compliance with study requirements.
- Uncontrolled thyroid disease, defined as free triiodothyronine (T3) and free thyroxine (T4) $> 3 \times$ ULN at screening.
- Uncontrolled diabetes defined as a fasting serum glucose $> 2 \times$ ULN or glycated hemoglobin levels $> 8.5\%$ at screening.
- Gastrointestinal (GI) tract disease resulting in an inability to take oral medication, malabsorption syndrome, a requirement for intravenous (IV) alimentation, prior surgical procedures affecting absorption, or uncontrolled inflammatory GI disease (eg, Crohn's, ulcerative colitis).
- Current active hepatic or biliary disease (exception of patients with Gilbert's syndrome, asymptomatic gallstones, liver metastases, or stable chronic liver disease per Investigator assessment).
- Ongoing peripheral neuropathy of Grade > 2 according to the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0.
- Severe and/or uncontrolled medical conditions or other conditions that could affect participation in the study such as:
 - Symptomatic congestive heart failure of New York Heart Association Class III or IV.
 - Unstable angina pectoris, symptomatic congestive heart failure, myocardial infarction within 6 months of start of study drug, serious uncontrolled cardiac arrhythmia, or any other clinically significant cardiac disease.
 - Liver disease, including cirrhosis and severe hepatic impairment.
- Active (acute or chronic) or uncontrolled severe infections.
- Known history of HIV, hepatitis B, or active hepatitis C virus at screening.
- Prior investigational anticancer therapy within 4 weeks prior to CAM-H2 administration.
- Patients who have had a major surgery or significant traumatic injury within 4 weeks of start of study drug, who have not recovered from side effects of any major surgery (defined as requiring general anesthesia), or have a major surgery planned during the course of the study.
- Other malignancies within the past 3 years except for adequately treated carcinoma of cervix or basal or squamous cell carcinomas of the skin or stage I uterine cancer.
- Radiation therapy for metastatic disease foci outside the brain, administered within 3 weeks before study enrollment.
- Known hypersensitivity to any of the study drugs, including inactive ingredients, including iodine allergy.
- History of significant comorbidities that, in the Investigator's judgement, may interfere with study conduct, response assessment, or informed consent.
- Unable or unwilling to complete the study procedures.
- Patients that cannot be hospitalized in a radionuclide therapy room.
- Patients that are unable to comply with thyroid protective pre-medication.
- Patients in whom bladder catheterization cannot be performed, or in patients who are unwilling to be catheterized if necessary.
- Patients with contraindications for undergoing MRI or CT, including for receiving contrast agents.
- Patient is the Investigator or sub-Investigator, research assistant, pharmacist, study coordinator,

or other staff or relative thereof, who is directly involved in the conduct of the study.